



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/697,563

10/31/2003

Najla Guthrie

21055-77

8415

28221 7590 04/15/2009
PATENT DOCKET ADMINISTRATOR
LOWENSTEIN SANDLER PC
65 LIVINGSTON AVENUE
ROSELAND, NJ 07068

EXAMINER

BETTON, TIMOTHY E

ART UNIT

PAPER NUMBER

1617

MAIL DATE

DELIVERY MODE

04/15/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/697,563	Applicant(s) GUTHRIE ET AL.	
	Examiner TIMOTHY E. BETTON	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26 and 27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 26 and 27 is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' Remarks filed on 29 December 2008 have been acknowledged and duly made of record.

Response to Arguments

Claim Rejections under 35 U.S.C. § 103(a) over Malterud et al. and Bok et al. are averred by applicants because of the alleged misinterpretation by Examiner with regard to art-known evidence of the varying potencies in polymethoxyflavones.

Accordingly, all of the rejected claims have been cancelled with the exception of 26 and 27. Applicants' claim that said claims are directed to methods of treating abnormalities resulting from insulin resistance with a polymethoxyflavone composition consisting of nobiletin and tangeretin.

Applicants claim that the limitations disclosed in claim s 26 and 27 overcome the claim rejections under 35 U.S.C. § 103(a) over Malterud et al. and Bok et al. because applicants' assert that the references are each directed to different fields of endeavor.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the references are sufficient for what they teach.

Manthey et al. has been reconsidered in view of the amendments to the current claims and current response and has been hereby withdrawn.

Further, applicants assert that claims 26 and 27 disclose a compact combination of a nobiletin and tangeretin in a formulation to treat metabolic abnormalities due to insulin insufficiency.

However, the broadness of the claim is still exemplified via the disclosure of *comprising* in reference to a method of oral administration, the two current amendments to reflect *consisting* /*consisting essentially of* notwithstanding. The comprising language in claim 26 does not overcome the rejection.

With regard to the claim 27, the art is replete with embodiments drawn to polymethoxyflavones disclosed *en masse* in native state or in a number of derived formulations. The same effect that a grouping of these polymethoxyflavones would have therapeutically would clearly be apparent to the one of skill if only two of these polymethoxyflavones were employed in view of the scope of the claimed invention.

Rejections not reiterated from previous Office Actions are hereby withdrawn . The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

For the reasons already made of record, the rejection is maintained.

Claim Rejection, 35 U.S.C. § 103(a)

Art Unit: 1617

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malterud et al. (Inhibitors of 15-lipoxygenase from orange peel. J Agric Food Chem (2000 Nov); 48(11): 5576-80, printed page: 1, Abstract, lines 1-6 and lines 17-21) in view of Bok et al. (USPN 6,096,364).

Malterud et al. teach the complete list of polymethoxylated flavonoids as disclosed in instant claim 15, such as sinensetin, nobiletin, tangeretin, heptamethoxyflavone and tetramethylscutellarein (as disclosed in instant claim 15), which have been isolated from orange peel and collectively are inhibitors of 15 lipoxygenase (lines 1-6).

Malterud et al. further teaches that [these] orange peel constituents may counteract enzymatic lipid peroxidation processes catalyzed by 15-lipoxygenase in vitro (lines 17-21).

Thus, Malterud et al. teach inhibitors of lipoxygenase, which is connected to Type 2 diabetes, which is consequently the disease to which insulin resistance progresses. Specifically, increased production of 15-lipoxygenase adversely affects insulin resistant/Type 2 diabetic patients. Insulin resistance is normally a precursor adverse affect, which progresses into Type 2 diabetic patients.

Art Unit: 1617

Malterud et al. do not teach a method for preventing insulin resistance nor does it teach on tetramethylscutellarein, a polymethoxylated flavone as disclosed in instant claim 15.

Bok et al. teach a method for lowering blood glucose levels in diabetic patients by the administration of bioflavonoid. The polymethoxylated flavones taught are nobiletin, sinensetin, and tangeretin (column 1, Table I).

Bok et al. do not specifically teach a method of reducing insulin resistance nor does it teach on tetramethylscutellarein or heptamethoxyflavone as disclosed in instant claim 15.

Thus, it is prima facie obvious to combine and/or incorporate together the teachings of Malterud et al. and Bok et al., via the motivation to combine by Malterud et al. Malterud et al. teach the complete disclosure of polymethoxylated flavones as disclosed in instant claim 15. As comprised in instant claim 15 for insulin resistance, the five disclosed polymethoxylated flavones are taught as a group comprising thereof for inhibition of 15-lipoxygenase. One of ordinary skill in the pertinent art at the time of the instant invention would instantly recognize the motivation to incorporate and modify the teachings of Bok et al. with the addition of Malterud et al. (incorporating the addition of tetramethylscutellarein). Accordingly, The radical –scavenging activity of the five instant polymethoxylated flavones disclosed results in a practicing method of reducing 15- lipoxygenase (Hatley et al. Increased production of 12/15 lipoxygenase eicosanoids accelerates monocyte/endothelial interactions in diabetic db/db mice. J Biol Chem. 2003 July 13; 278(28): 25369-75, printed pages 1 and 2, see page 1)

Malterud et al. is the motivation to combine due to 1) the five identical bioflavonoid agents as disclosed and taught in instant invention and Malterud et al., and 2) the five identical bioflavonoid agents with indication of therapy for inhibiting an enzyme, which has direct

Art Unit: 1617

correlation to insulin resistance as disclosed in instant invention. This rejection is necessitated by amendment.

Thus it would have been obvious to one of ordinary skill in the pertinent art at the time of the invention to have modified and/or combined the methods and teachings of Robbins and Pershadsingh et al. The instant invention is drawn toward a method of treating a mammal having metabolic abnormalities resulting from insulin resistance comprising administering an effective amount of polymethoxyflavone composition comprising sinensetin, nobiletin, tangeretin, heptamethoxyflavone and tetramethylscutellarein to reduce serum insulin levels by at least about 26% (instant claim 15). One of ordinary skill in the art would have had a reasonable expectation of successfully combining and/or modifying Robbins and Pershadsingh et al. which both essentially teach practicing polymethoxylated flavones and methods of administration thereof. This rejection is necessitated by amendment.

Further, in view of all references cited *supra*, the deficiencies of the Malterud et al. reference are adequately elucidated by Bok et al. Malterud et al adequately satisfy the deficiencies of Bok et al. Malterud et al. essentially teaches each and every polymethoxyflavonoid in view of the instant invention. Further motivation to combine is contained in the following:

“It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information

Art Unit: 1617

about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617